AFOR

Atty. Dkt. No. 029318-0109

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Bosch et al.

Title: ***DRY POWDER AEROSOLS OF NANOPARTICULATE DRUGS***

Appl. No.: 09/190,138

Filing Date: November 12, 1998

Examiner: R.O. Berko

Art Unit: 1615

TRANSMITTAL OF BRIEF ON APPEAL

Mail Stop APPEAL BRIEF-PATENTS
Commissioner for Patents
PO Box 1450
Alexandria, Virginia 22313-1450

Sir:

Transmitted herewith is an appeal brief in the above-identified application:

Submitted herewith in connection with the above application are the following:

[X] Brief on Appeal, original and two (2 copies).

[X] A check in the amount of $340.00 is enclosed in payment of fee for filing a brief in support of an appeal under 37 CFR 1.17(c).

[X] Applicant hereby petitions for an extension of time under 37 C.F.R. §1.136(a) for the total number of months checked below:

[X]	Extension for response filed within the first month:	$110.00		$110.00

[X] A check in the amount of $450.00 is enclosed in payment of fee for filing a brief in support of an appeal under 37 CFR 1.17(c).

[ ] Please charge Deposit Account No. 19-0741 in the amount of $00.00. A duplicate copy of this transmittal is enclosed.

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[X] The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Please direct all correspondence to the undersigned attorney or agent at the address indicated below.

Respectfully submitted,

Date October 13, 2004

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Applicant: Bosch et al.

Title: ***DRY POWDER AEROSOLS OF NANOPARTICULATE DRUGS***

Appl. No.: 09/190,138

Filing Date: 11/12/1998

Examiner: R. O. Berko

Art Unit: 1615

APPELLANT'S BRIEF ON APPEAL UNDER 37 C.F.R. § 41.37

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Under the provisions of 37 C.F.R. § 41.37, this Appeal Brief is being filed together with a check in the amount of $340.00 covering the Rule 17(c) appeal fee. If this fee is deemed to be insufficient, authorization is hereby given to charge any deficiency (or credit any balance) to the undersigned deposit account 19-0741.

I. REAL PARTY IN INTEREST

The real party in interest is ELAN PHARMA INTERNATIONAL, LTD. The inventors assigned their right, title, and interest in this application to NANOSYSTEMS on January 6 and 11, 1999. This assignment was recorded in the U.S. Patent and Trademark Office at Reel 009861, Frame 0227. NANOSYSTEMS subsequently assigned its right, title, and interest in this application to ELAN PHARMA INTERNATIONAL, LTD. This assignment was recorded in the U.S. Patent and Trademark Office at Reel 011079, Frame 0301.

II. RELATED APPEALS AND INTERFERENCES

There are no appeals or interferences related to the present application.

III. STATUS OF CLAIMS

Pending claims: 11-36, 40-45, 47-49, and 51-121.

Canceled claims: 1-10, 37-39, 46, and 50.

Rejected claims: 11-36, 40-45, 47-49, and 51-121.

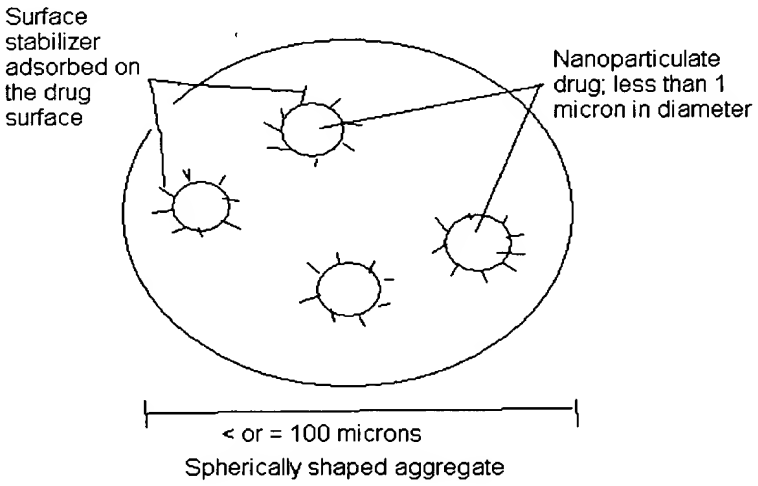
Appealed claims: 11-36, 40-45, 47-49, and 51-121.

IV. STATUS OF AMENDMENTS

An after-final response, filed on May 14, 2004, sought to amend independent claims 11, 23, 35, 40, and 42-44. In light of the Advisory Action dated July 22, 2004, Appellants understand that the amendments will be entered for purposes of the present appeal. Consequently, the appended claims reflect entry of the amendments.

V. SUMMARY OF THE CLAIMED SUBJECT MATTER

The claimed invention is directed to dry powder aerosol compositions of nanoparticulate crystalline drugs for pulmonary and nasal delivery and to methods of making and using the compositions. *See* specification at page 7, lines 24-25; and page 16, lines 11-12. The claimed compositions comprise spherically-shaped aggregates of crystalline drug nanoparticles having a surface modifier adsorbed to the surface thereof. *Id.* at page 17, lines 6-7; page 20, lines 23; and page 33, line 16. The drug particles must be crystalline (*id.* at page 24, lines 26-28), and exhibit an effective average particle size of less than about 1 micron. *Id.* at page 7, lines 5-6; and page 13, lines 2-8. The diameters of the spherically-shaped aggregates are equal to or less than about 100 microns. *Id.* at page 17, lines 10-18. The compositions are graphically shown below.



Finally, the aggregates must yield back the nanoparticulate drug particles in a dispersion upon reconstitution in an aqueous medium. *Id.* at page 8, line 28; page 9, line 17; page 33, lines 19-22; and page 34, lines 28-30.

Appellants' discovery is a substantial advance over conventional micronized drug formulations that are intended for delivery to the pulmonary and nasal regions. The nanoparticulate drug particle size facilitates the drug particles' fitting into a wide aggregate particle size range. Consequently, in contrast to conventional micronized formulations, aggregate particles of the invention measuring less than about 2 microns up to about 100 microns uniformly contain the same concentration of nanoparticulate drug particles. This enables more effective and efficient drug delivery to a desired region. *See* specification at page 23, line 26, to page 24, line 6.

Moreover, the claimed invention results in more favorable drug delivery profiles relative to micronized drugs as the nanoparticulate drug size enables more concentrated unit doses. *Id.* at page 23, lines 17-22. Additionally, a number of advantageous bulk properties result from the claimed compositions. For example, the claimed compositions can be nebulized ultrasonically whereas micronized drug dispersions cannot. *Id.* at page 23, lines 23-25. Finally, in contrast to micronized drugs, the claimed invention enables very rapid drug delivery to pulmonary and nasal surfaces. *Id.* at page 24, lines 7-10 and 15-18.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Four grounds of rejections remain after the issuance of the Final Office Action dated January 14, 2004:

A. Whether claims 11-34, 40, 41, 44, 45, 47, 48, 51-62, 69-96, and 111-119 are unpatentable under 35 U.S.C. § 103(a) over U.S. Patent No. 5,985,309 to Edwards et al. ("Edwards").

B. Whether claims 11-34, 40- 45, 47, 48, 51-62, 65-96, and 97-119 are unpatentable under 35 U.S.C. § 103(a) over Edwards in view of U.S. Patent No. 5,145,684 to Liversidge et al. ("Liversidge").

C. Whether claims 35, 36, 49, 63, and 64 are unpatentable under 35 U.S.C. § 103(a) over Edwards in view of U.S. Patent No. 5,202,110 to Dalby et al. ("Dalby").

D. Whether claims 120 and 121 are unpatentable under 35 U.S.C. § 103(a) over Edwards in view of Goodman & Gilman's, *The Pharmacological Basis of Therapeutics*, Ninth edition, page 666 (McGraw-Hill, 1996) ("Goodman").

VII. ARGUMENT

As described in more detail below, *none* of the cited references, either alone or in combination, teach or suggest the following elements required by each of Appellants' claims:

(1) *spherically-shaped aggregates* of drug nanoparticles having a surface modifier adsorbed to the surface thereof,

(2) *crystalline* drug nanoparticles;

(3) drug particles having an effective average particle size of *less than about 1 micron*, and

(4) spherically-shaped aggregates that *redisperse into nanoparticulate drug particles* upon reconstitution in an aqueous medium.

It will therefore be shown that the claimed invention is patentable over the cited references, as "[o]bviousness requires a suggestion of all elements in a claim." *In re Royka*, 490 F. 2d 981 (CCPA 1974).

A. Ground 1: Claims 11-34, 40, 41, 44, 45, 47, 48, 51-62, 69-96, and 111-119 are Patentable under 35 U.S.C. § 103(a) over Edwards

Edwards does not teach or suggest each limitation of the claimed invention, nor would a person of ordinary skill in the art have been motivated to modify the reference in a manner such as to arrive at the claimed invention.

1. Edwards Does not Teach or Suggest Nanoparticulate Sized Drug Particles, As Required by the Claimed Invention

Edwards refers to *microparticulate* drug compositions for administration to the respiratory tract via an aerosol formulation. *See* Edwards at col. 3, lines 1-3; and col. 5, lines 29-33. Specifically, the disclosed aerosol particles have "a mean diameter of between approximately 5 μm and 30 μm." Edwards at col. 6, lines 1-7. Additionally, Edwards discloses a number of processes for making particles that satisfy these size requirements. *See e.g.*, Edwards at col. 8., lines 5-29. None of the disclosed particles nor the processes for making them remotely suggest that the particles comprise *nanoparticulate* drug particles.

The PTO recognized that "Edwards et al. do not specifically state that 50% of the [disclosed] particles have a geometric particle size of less than about 1 μm [as claimed]." Office Action, dated February 5, 2001, at page 5. Nonetheless, it is the "examiner's position that Edwards disclosed that nanosize drug particles in aerosol form were delivered to the alveoli of the lungcol 3 [*sic*; "lung, col. 3], lin 330-35 [*sic*; "33-35"] and col 5, lin 30-40."

Edwards simply teaches nothing of the sort. *See* Appellants' Response, dated May 14, 2004, at pages 23-24. Edwards teaches that "[a]dministration by aerolization permits deep lung delivery of *relatively large diameter* therapeutic aerosols, for example, greater than *5 μm in mean diameter*." Edwards at col. 5, lines 31-34 (emphasis supplied). Thus, Edwards flatly refutes the PTO's contention that the reference teaches nanoparticulate drug particles on account of drug particles reaching the deep lung.

2. Edwards Teaches Away From Appellants' Claimed Aggregates Comprising Nanoparticulate Drug Particles

In addition to failing to teach nanoparticulate drug particles, Edwards teaches *away* from utilizing such small drug particles in the described compositions. Specifically, Edwards suggests that nanoparticulate drug particles would be ineffective for delivery of a drug to the pulmonary system. This is significant, as "references that teach away cannot serve to create a prima facie case of obviousness." *McGinley v. Franklin Sports, Inc.*, 262 F. 3d 1339, 1354 (Fed. Cir. 2001) (citing *In re Gurley*, 27 F. 3d 551, 553 (Fed. Cir. 1994)).

Edwards teaches that larger drug particles, *e.g.*, those having a mean diameter between 5μm and 30 μm, are used to provide maximum deposition of the drug within the lungs. *See* Edwards at col. 5, lines 10-15. Moreover, the larger particles of Edwards avoid the fate of "very small particles of less than five microns in diameter, preferably between one and three microns in diameter, which are then subject to phagocytosis." Edwards at col. 5, lines 16-18.

Edwards thus teaches that inhalation of larger, not smaller, drug particles are necessary for delivery of the drug to the lungs to avoid the risk of phagocytosis. Consequently, a person of ordinary skill in the art would have been counseled by Edwards *against* making smaller drug particles for their delivery to the lung, as required by the claimed invention. The person therefore would not have been motivated to make Appellants' claimed invention comprising nanoparticulate drug particles.

3. Edwards Does Not Teach or Suggest *Crystalline* Drug Nanoparticles, As Required by the Claimed Invention

Edwards does not teach or suggest that the drug must be crystalline, as required by each of Appellants' claims. Edwards teaches several methods of manufacturing the disclosed drug microparticles, including emulsion solvent evaporation and spray drying, each of which result in *amorphous* drug substances. *See* Appellants' Response dated July 11, 2002 at page 6. *See also*

Edwards at col. 8, lines 7-10; col. 13, lines 49 to col. 14, line 19 (Example 1; evaporation); col. 14, lines 21 to 49 (Example 2; spray-drying).

Thus, in contrast to the amorphous particles of Edwards, Appellants' claimed invention comprises crystalline drug nanoparticles. Moreover, no motivation or suggestion is provided within Edwards to modify the described compositions to utilize crystalline drug.

4. Edwards Does not Teach or Suggest Spherically Shaped Aggregates, as Required by the Claimed Invention

Appellants' claimed invention is further patentable over Edwards because the reference does not teach or suggest aggregates that are spherically-shaped, as required by each of Appellant's claims. In particular, the microparticles of Edwards are "rough (non-smooth) [and] non-spherical . . ." Edwards at col. 9, lines 15-17.

Moreover, the PTO has indicated no motivation for one of ordinary skill in the art to modify the rough particles of Edwards to obtain the smooth particles of the claimed invention. *See* Appellants' Response dated May 14, 2004 at page 22.

Furthermore, Edwards teaches away from Appellants' claimed invention because the reference emphasizes that the aerodynamic lightness of the disclosed particles is achieved in part by creating irregular surface structures on the particles.

Thus, in contrast to the rough particles of Edwards, Appellants' claimed invention comprises smooth spherical aggregates of drug nanoparticles. Moreover, no motivation or suggestion is provided within Edwards to modify the described compositions to utilize smooth spherical aggregates of drug particles.

5. Edwards Does Not Teach or Suggest Aggregates That Yield Nanoparticulate Drug Dispersions Upon Reconstitution in an Aqueous Media, in Contrast to the Claimed Invention

Edwards does not teach or suggest that the described aggregates of microparticulate drug particles form nanoparticulate drug particle dispersions upon reconstitution in an aqueous medium. *See* Appellants' Response dated May 14, 2004 at page 25. In fact, Edwards teaches instead that the disclosed large and aerodynamically light drug particles simply "undergo slow degradation and drug release." Edwards at col. 10, lines 37-38.

6. The PTO Invoked an Improper Legal Standard in Requiring Appellants' to Demonstrate in Comparative Tests That the Claimed Compositions are Superior to those of Edwards

The PTO invoked an incorrect legal standard in requiring Appellants to demonstrate via experiments that the claimed compositions are superior to those of Edwards. A "superior" formulation is not the standard of patentability; rather, Appellants' burden is to show that the claimed composition is not anticipated or obviated by the cited reference by demonstrating that Edwards does not teach or suggest each and every element of the claimed invention. As detailed above, Appellants' have met their burden.

7. Conclusion

Because Edwards does not teach or suggest all of the limitations of Appellants' claims, and because the PTO has failed to identify a suggestion or motivation to modify Edwards to arrive at the claimed invention, this ground for rejection should be reversed.

B. Ground 2: Claims 11-34, 40- 45, 47, 48, 51-62, 65-96, and 97-119 are Patentable under 35 U.S.C. § 103(a) over Edwards in view of Liversidge

Edwards in combination with Liversidge does not obviate the claimed invention because Liversidge does not remedy any of deficiencies of Edwards discussed above, and because the references militate against making the claimed aerosol composition.

1. Summary of the Cited References

Liversidge is directed to a composition of a "crystalline drug substance having a surface modifier adsorbed on the surface thereof . . . to maintain an effective average particle size of less than about 400 nm." Liversidge at col. 2, lines 38-43. The nanoparticulate compositions of Liversidge are disclosed as being useful in oral, parenteral, and intravenous administration applications. *See* Liversidge at col. 8, lines 10-13.

In contrast to the teachings of Liversidge, Edwards discloses "aerodynamically light particles generally hav[ing] a mean diameter between 5 μm and 30 μm", Edwards at col. 4, lines 1-4, for "delivery of a therapeutic agent to the airways of the alveolar region of the lung." *Id.* at col. 4, lines 19-20.

The cited references thus embody: (1) non-obvious variants of drug compositions and (2) non-overlapping routes of administration. Neither reference suggests Appellants' claimed aggregate

of nanoparticulate drug dispersions nor does the PTO demonstrate how one of ordinary skill in the art would modify the light particles of Edwards with the comparatively dense crystalline particles of Liversidge to arrive at the claimed invention.

2. Edwards Teaches Away from Combining the Teaching with that of Liversidge

Edwards teaches away from the claimed invention because the reference teaches that small drug particles are not useful in the context of pulmonary drug delivery. "If references taken in combination would produce a 'seemingly inoperative device,' . . . such references teach away from the combination and thus cannot serve as predicates for a prima facie case of obviousness." *See McGinley v. Franklin Sports, Inc.*, 262 F. 3d 1339, 1354 (Fed. Cir. 2001) (quoting *In re Sponnoble*, 405 F. 2d 578, 587 (CCPA 1969)).

As noted above, Edwards is directed to large drug particles, *i.e.*, 5 μm to 30 μm, to avoid the fate of "very small particles of less than five microns in diameter, preferably between one and three microns in diameter, which are then subject to phagocytosis." Edwards at col. 5, lines 16-18. A person of ordinary skill in the art would therefore have been dissuaded by Edwards from using the nanoparticulate compositions of Liversidge in a modification of Edwards to arrive at the claimed dry powder aerosol.

3. In Contrast to the PTO's Assertion, Edwards Does Not Teach Nanoparticulate Drug Particles

The PTO propounded two theories in fortifying the ground for maintaining this rejection. The facts in this case support neither theory. First, the PTO pronounced that "the disclosures in Leversidge [*sic*, "Liversidge"] . . . are in the same field of endeavor as that in Edwards – nanosize drug particles that are surface modified in liquid dispersion." Office Action dated January 14, 2004 at page 4. Appellants have pointed out that Edwards and Liversidge are *not* both directed to nanoparticulate drug particles. *See* Appellants' Response dated May 14, 2004 at page 27. Specifically, as discussed above, Edwards does not teach or suggest drug nanoparticles.

Second, the PTO styled Liversidge as "address[ing] similar problems that were raised in Edwards concerning nanosize drug delivery formulations through the respiratory tract . . ." Even a cursory inspection of Liversidge indicates that this is not so. Thus Appellants' emphasize here, *supra*, as before that Liversidge teaches "that the pharmaceutical compositions of this invention will be particularly useful in oral and parenteral, including intravenous, administration applications."

Liversidge at col. 8, lines 10-13. Liversidge simply does not address the administration of "nanosize drug delivery formulations through the respiratory tract." Office Action dated January 14, 2004 at page 4.

4. Conclusion

The proposed combination of Edwards and Liversidge therefore does not teach or suggest all of the limitations of Appellants' claims, specifically the recited aggregates comprising nanoparticulate drug dispersions. Moreover, Edwards teaches away from the combination because the reference specifically teaches the inoperability of the aerosol delivery of small drug particles. For these reasons, the combination of references does not obviate the claimed invention. Consequently, Appellants respectfully request the Board to reconsider and reverse this ground for rejection.

C. Ground 3: Claims 35, 36, 49, 63, and 64 are unpatentable under 35 U.S.C. § 103(a) over Edwards in view of Dalby

The combination of Edwards and Dalby does not obviate the claimed invention because Dalby fails to remedy the deficiencies of Edwards.

The PTO cites Dalby "for teaching propellant metered dose inhalers where the propellant is a 'non-CFC' propellant." *See* Office Action dated December 24, 2004 at page 4. *See also* Office Action dated January 14, 2004 at page 4.

Dalby, as with Edwards, does not teach or suggest aggregates of crystalline, nanoparticulate drug particles as required by each of Appellants' claims. Dalby is directed to formulations of beclomethasone diproprionate for aerosol delivery *via* a metered dose inhaler. *See* Dalby at col. 2, lines 22-26. In particular, the reference teaches that "the micronized drug . . . should be easily dispersible in the propellant or propellant blend with the aid of a surfactant, or completely dissolve." *Id.* at col. 2, lines 36-38.

Dalby therefore does not teach or suggest that the disclosed drug particles are or should be crystalline, much less that the particles form spherically-shaped aggregates measuring less than or equal to about 100 microns in diameter as claimed.

Because Edwards in combination with Dalby does not teach or suggest each and every element of the claimed invention, Appellants respectfully request the Board to reconsider and reverse this ground for rejection.

D. Issue 4: Claims 120 and 121 are Patentable under 35 U.S.C. § 103(a) over Edwards in view of Goodman

The combination of Edwards and Goodman also fails to teach or suggest the claimed invention because Goodman does not remedy the deficiencies of Edwards, discussed above.

The PTO relied upon Goodman to the extent that the reference "teaches . . . beclomethasone dipropionate . . . [as a] steroid administered for asthma in aerosol formulations." Office Action dated December 24, 2002 at page 6.

Goodman does not address the requisite: (1) spherically-shaped aggregates of drug nanoparticles having a surface modifier adsorbed to the surface thereof, (2) crystalline drug nanoparticles, (3) drug nanoparticles having an effective average particle size of less than about 1 micron, or (4) spherically-shaped aggregates that redisperse into nanoparticulate drug particles upon reconstitution in an aqueous medium. Because Edwards also does not teach or suggest any of these claimed features of Appellants' invention, the combination of Edwards and Goodman also fails to do so.

Because Edwards in combination with Goodman does not teach or suggest all of the claimed features of Appellants' invention, and because Goodman does not suggest modifying Edwards to arrive at the claimed invention, Appellants respectfully request the Board to reconsider and reverse this ground for rejection.

VIII. CONCLUSION

Edwards, alone or in combination with any of the cited secondary references, does not teach or suggest the claimed dry powder aerosol comprising spherically-shaped aggregates of crystalline, submicron-sized drug nanoparticles. Edwards specifically teaches away from the use of smaller drug particles and spherically-shaped particles. None of the secondary references cure these deficiencies of Edwards, or at least suggest that the compositions of Edwards be modified. For all of these reasons, Appellants courteously request the Board to reconsider and reverse all grounds for rejection of the claims.

Respectfully submitted,

Date Oct 13, 2004

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CLAIMS APPENDIX

1. – 10. (cancelled).

11. (Currently Amended) A dry powder aerosol composition for pulmonary or nasal delivery comprising spherically shaped aggregates ~~of~~ formed from spray-drying aqueous dispersions of nanoparticulate drug particles, wherein:

(a) the aqueous dispersions of nanoparticulate drug particles:

(i) comprise a poorly soluble crystalline drug, wherein by "poorly soluble" it is meant that the drug has a solubility in at least one liquid dispersion medium of less than about 10 mg/ml,

(ii) have an effective average particle size of less than about 1000 nm, meaning at least 50% of the drug particles have a particle size of less than about 1000 nm, and

(iii) have a surface modifier adsorbed on the surface thereof; and

(b) the aggregates of such spray-dried drug particle dispersions are less than or equal to about 100 microns in diameter; and

(c) such aggregates return to nanoparticulate drug particle dispersions upon reconstitution in an aqueous liquid medium.

12. (Original) The aerosol composition of claim 11 further comprising a diluent.

13. (Original) The aerosol composition of claim 12, wherein essentially every diluent particle comprises at least one embedded nanoparticulate drug particle having a surface modifier adhered to the surface of the drug particle.

14. (Original) The aerosol composition of claim 11, wherein the drug is selected from the group consisting of proteins, peptides, elastase inhibitors, analgesics, cystic-fibrosis therapies, asthma therapies, emphysema therapies, respiratory distress syndrome therapies, chronic bronchitis therapies, chronic obstructive pulmonary disease therapies, organ-transplant rejection therapies, therapies for tuberculosis and other infections of the lung, fungal infection therapies, and respiratory illness therapies associated with acquired immune deficiency syndrome, an oncology drug, an anti-emetic, and a cardiovascular agent.

15. (Previously Presented) The aerosol composition of claim 11, wherein the nanoparticulate drug particles have an effective average particle size of less than about 400 nm.

16. (Original) The aerosol composition of claim 11, wherein the aerosol comprises a concentration of a drug in an amount of from about 0.05 mg/g up to about 900 mg/g.

17. (Original) The aerosol composition of claim 16, wherein the aerosol comprises a concentration of a drug selected from the group consisting of about 10 mg/g or more, about 100 mg/g or more, about 200 mg/g or more, about 400 mg/g or more, about 600 mg/g or more, and about 900 mg/g.

18. (Previously Presented) The aerosol composition of claim 11, wherein the aggregates of the nanoparticulate drug particles have a mass median aerodynamic diameter of about 2 to about 10 microns.

19. (Previously Presented) The aerosol composition of claim 18, wherein the aggregates of the nanoparticulate drug particles have a mass median aerodynamic diameter of about 2 to about 6 microns.

20. (Previously Presented) The aerosol composition of claim 11, wherein the aggregates of the nanoparticulate drug particles have a mass median aerodynamic diameter of less than about 2 microns.

21. (Previously Presented) The aerosol composition of claim 11, wherein the aggregates of the nanoparticulate drug particles have a mass median aerodynamic diameter of about 5 to about 100 μm.

22. (Previously Presented) The aerosol composition of claim 21, wherein the aggregates of the nanoparticulate drug particles have a mass median aerodynamic diameter of about 30 to about 60 μm.

23. (Currently Amended) A dry powder aerosol composition for pulmonary or nasal delivery comprising spherically shaped aggregates formed from freeze-drying aqueous dispersions of nanoparticulate drug particles, wherein:

(a) the aggregates of such freeze-dried drug particle dispersions are less than or equal to about 100 microns in diameter;

(b) the aqueous dispersions of nanoparticulate drug particles:

(i) comprise a poorly soluble crystalline drug, wherein by "poorly soluble" it is meant that the drug has a solubility in at least one liquid dispersion medium of less than about 10 mg/ml,

(ii) have an effective average particle size of less than about 1000 nm, meaning at least 50% of the drug particles have a particle size of less than about 1000 nm, and

(iii) have a surface modifier adsorbed on the surface thereof; and

(c) such aggregates return to nanoparticulatre drug particle dispersions upon reconstitution in an aqueous liquid medium.

24. (Original) The aerosol composition of claim 23, further comprising a diluent.

25. (Previously Presented) The aerosol composition of claim 23, wherein the drug is selected from the group consisting of proteins, peptides, elastase inhibitors, analgesics, cystic-fibrosis therapies, asthma therapies, emphysema therapies, respiratory distress syndrome therapies, chronic bronchitis therapies, chronic obstructive pulmonary disease therapies, organ-transplant rejection therapies, therapies for tuberculosis and other infections of the lung, fungal infection therapies, and respiratory illness therapies associated with acquired immune deficiency syndrome, an oncology drug, an anti-emetic, and a cardiovascular agent.

26. (Previously Presented) The aerosol composition of claim 23, wherein the nanoparticulate drug particles have an effective average particle size of less than about 400 nm.

27. (Original) The aerosol composition of claim 23, wherein the aerosol comprises a concentration of a drug in an amount of from about 0.05 mg/g up to about 900 mg/g.

28. (Original) The aerosol composition of claim 27, wherein the aerosol comprises a concentration of a drug selected from the group consisting of about 10 mg/g or more, about 100 mg/g or more, about 200 mg/g or more, about 400 mg/g or more, about 600 mg/g or more, and about 900 mg/g.

29. (Previously Presented) The aerosol composition of claim 23, wherein the aggregates of the nanoparticulate drug particles have a mass median aerodynamic diameter of about 2 to about 10 microns.

30. (Previously Presented) The aerosol composition of claim 29, wherein the aggregates of the nanoparticulate drug particles have a mass median aerodynamic diameter of about 2 to about 6 microns.

31. (Previously Presented) The aerosol composition of claim 23, wherein the aggregates of the nanoparticulate drug particles have a mass median aerodynamic diameter of less than about 2 microns.

32. (Previously Presented) The aerosol composition of claim 23, wherein the aggregates of the nanoparticulate drug particles have a mass median aerodynamic diameter of about 5 to about 100 μm.

33. (Previously Presented) The aerosol composition of claim 32, wherein the aggregates of the nanoparticulate drug particles have a mass median aerodynamic diameter of about 30 to about 60 μm.

34. (Original) The aerosol composition of claim 23, further comprising spray-dried nanoparticulate drug powder, wherein the drug of the freeze-dried nanoparticulate drug powder is either the same or different from the drug of the spray-dried nanoparticulate drug powder.

35. (Currently Amended) A dry powder nanoparticulate aerosol composition for use in a propellant-based pMDI comprising

(a) spherically shaped aggregates of ~~a~~ nanoparticulate poorly soluble crystalline drug particles, wherein by "poorly soluble" it is meant that the drug has a solubility in at least one liquid dispersion medium of less than about 10 mg/ml, wherein the aggregates are less than or equal to about 100 microns in diameter, wherein such aggregates return to nanoparticulate drug particles upon reconstitution in an aqueous liquid medium, and wherein the drug particles:

(i) have a surface modifier adsorbed on the surface thereof, and

(ii) have an effective average particle size of less than about 1000 nm, meaning at least 50% of the drug particles have a particle size of less than about 1000 nm, and

(b) a non-aqueous propellant.

36. (Original) The aerosol composition of claim 35, wherein the propellant is a non-CFC propellant.

37. – 39. (Cancelled)

40. (Currently Amended) A method of making a dry powder nanoparticulate drug composition comprising:

(a) forming an aqueous nanoparticulate dispersion of a poorly soluble drug, wherein:

(i) the dispersion comprises poorly soluble crystalline drug particles and a surface modifier adsorbed on the surface thereof, wherein by "poorly soluble" it is meant that the drug has a solubility in the liquid dispersion medium of less than about 10 mg/ml, and

(ii) the drug particles have an effective average particle size of less than about 1000 nm, meaning at least 50% of the drug particles have a particle size of less than about 1000 nm; and

(b) spray-drying the nanoparticulate dispersion to form a dry powder of spherically shaped aggregates of the nanoparticulate drug and surface modifier particles, wherein the aggregates have a diameter of less than or equal to about 100 microns, and wherein such aggregates return to a nanoparticulate drug dispersion upon reconstitution in an aqueous liquid medium.

41. (Original) The method of claim 40, further comprising adding a diluent to the nanoparticulate dispersion prior to spray-drying, wherein following spray-drying essentially every diluent particle contains at least one embedded drug particle and a surface modifier.

42. (Currently Amended) A method of making a dry powder nanoparticulate drug aerosol formulation comprising:

(a) milling under non-pressurized conditions in a non-aqueous medium having a high boiling point a dispersion comprising the following:

(i) a poorly soluble crystalline drug, wherein by "poorly soluble" it is meant that the drug has a solubility in the non-aqueous medium of less than about 10 mg/ml, and

(ii) a surface modifier, to obtain a nanoparticulate drug composition having an effective average particle size of less than about 1000 nm, meaning at least 50% of the drug particles have a particle size of less than about 1000 nm, and

(b) evaporating the non-aqueous medium to obtain a dry powder of spherically shaped aggregates of drug and surface modifier particles, wherein the aggregates have a diameter of less than or equal to about 100 microns, and wherein such aggregates return to nanoparticulate drug particle dispersions upon reconstitution in an aqueous liquid medium.

43. (Currently Amended) A method of making an aerosol composition comprising:

(a) milling under pressurized conditions in a non-aqueous medium a dispersion comprising the following:

(i) a poorly soluble crystalline drug, wherein by "poorly soluble" it is meant that the drug has a solubility in the non-aqueous dispersion medium of less than about 10 mg/ml, and

(ii) a surface modifier, to obtain a drug having an effective average particle size of less than about 1000 nm, meaning at least 50% of the drug particles have a particle size of less than about 1000 nm;

(b) evaporating the non-aqueous medium to obtain a dry powder of spherically shaped aggregates of drug and surface modifier particles, wherein the aggregates have a diameter of less than or equal to about 100 microns, and wherein such aggregates return to nanoparticulate drug particle dispersions upon reconstitution in an aqueous liquid medium; and

(c) formulating the dry powder spherically shaped aggregates into an aerosol composition.

44. (Currently Amended) A method of making a dry powder nanoparticulate drug composition comprising:

(a) forming an aqueous nanoparticulate dispersion of a poorly soluble drug, wherein:

(i) the dispersion comprises poorly soluble crystalline drug particles, wherein by "poorly soluble" it is meant that the drug has a solubility in the liquid dispersion medium of less than about 10 mg/ml, and wherein the drug particles have an effective average particle size of less than about 1000 nm, meaning at least 50% of the drug particles have a particle size of less than about 1000 nm, and

(ii) a surface modifier adsorbed on the surface thereof; and

(b) freeze-drying the nanoparticulate dispersion to form a dry powder of spherically shaped aggregates of the nanoparticulate drug and surface modifier particles, wherein the aggregates have a diameter of less than or equal to about 100 microns, and wherein such aggregates return to nanoparticulate drug particle dispersions upon reconstitution in an aqueous liquid medium.

45. (Original) The method of claim 44, further comprising adding a diluent to the nanoparticulate dispersion prior to freeze-drying, wherein following freeze-drying essentially every diluent particle contains at least one embedded drug particle and a surface modifier.

46. (Cancelled).

47. (Original) A method of administering the aerosol of claim 11 to a patient, wherein the aerosol comprises drug at a concentration of 10 mg/g or greater, and wherein the patient delivery time for the aerosol administration is about 15 seconds or less.

48. (Original) A method of administering the aerosol of claim 23 to a patient, wherein the aerosol comprises drug at a concentration of 10 mg/g or greater, and wherein the patient delivery time for the aerosol administration is about 15 seconds or less.

49. (Original) A method of administering the aerosol of claim 35 to a patient, wherein the aerosol comprises drug at a concentration of 10 mg/g or greater, and wherein the patient delivery time for the aerosol administration is about 15 seconds or less.

50. (Cancelled).

51. (Previously Presented) The aerosol composition of claim 11, wherein the nanoparticulate drug particles have an effective average particle size of less than about 300 nm.

52. (Previously Presented) The aerosol composition of claim 11, wherein the nanoparticulate drug particles have an effective average particle size of less than about 250 nm.

53. (Previously Presented) The aerosol composition of claim 11, wherein the nanoparticulate drug particles have an effective average particle size of less than about 100 nm.

54. (Previously Presented) The aerosol composition of claim 11, wherein the nanoparticulate drug particles have an effective average particle size of less than about 50 nm.

55. (Previously Presented) The aerosol composition of claim 23, wherein the nanoparticulate drug particles have an effective average particle size of less than about 300 nm.

56. (Previously Presented) The aerosol composition of claim 23, wherein the nanoparticulate drug particles have an effective average particle size of less than about 250 nm.

57. (Previously Presented) The aerosol composition of claim 23, wherein the nanoparticulate drug particles have an effective average particle size of less than about 100 nm.

58. (Previously Presented) The aerosol composition of claim 23, wherein the nanoparticulate drug particles have an effective average particle size of less than about 50 nm.

59. (Previously Presented) The aerosol composition of claim 11, wherein at least 70% of the drug particles have a particle size of less than about 1000 nm.

60. (Previously Presented) The aerosol composition of claim 11, wherein at least 90% of the drug particles have a particle size of less than about 1000 nm.

61. (Previously Presented) The aerosol composition of claim 23, wherein at least 70% of the drug particles have a particle size of less than about 1000 nm.

62. (Previously Presented) The aerosol composition of claim 23, wherein at least 90% of the drug particles have a particle size of less than about 1000 nm.

63. (Previously Presented) The aerosol composition of claim 35, wherein at least 70% of the drug particles have a particle size of less than about 1000 nm.

64. (Previously Presented) The aerosol composition of claim 35, wherein at least 90% of the drug particles have a particle size of less than about 1000 nm.

65. (Previously Presented) The aerosol composition of claim 42, wherein at least 70% of the drug particles have a particle size of less than about 1000 nm.

66. (Previously Presented) The aerosol composition of claim 42, wherein at least 90% of the drug particles have a particle size of less than about 1000 nm.

67. (Previously Presented) The aerosol composition of claim 43, wherein at least 70% of the drug particles have a particle size of less than about 1000 nm.

68. (Previously Presented) The aerosol composition of claim 43, wherein at least 90% of the drug particles have a particle size of less than about 1000 nm.

69. (Previously Presented) The aerosol composition of claim 44, wherein at least 70% of the drug particles have a particle size of less than about 1000 nm.

70. (Previously Presented) The aerosol composition of claim 44, wherein at least 90% of the drug particles have a particle size of less than about 1000 nm.

71. (Previously Presented) The aerosol composition of claim 19, wherein the drug is selected from the group consisting of proteins, peptides, elastase inhibitors, analgesics, cystic-fibrosis therapies, asthma therapies, emphysema therapies, respiratory distress syndrome therapies, chronic bronchitis therapies, chronic obstructive pulmonary disease therapies, organ-transplant rejection therapies, therapies for tuberculosis and other infections of the lung, fungal infection therapies, and respiratory

illness therapies associated with acquired immune deficiency syndrome, an oncology drug, an anti-emetic, and a cardiovascular agent.

72. (Previously Presented) The aerosol composition of claim 19, wherein the nanoparticulate drug particles have an effective average particle size selected from the group consisting of less than about 400 nm, less than about 300 nm, less than about 250 nm, less than about 100 nm, and less than about 50 nm.

73. (Previously Presented) The aerosol composition of claim 20, wherein the drug is selected from the group consisting of proteins, peptides, elastase inhibitors, analgesics, cystic-fibrosis therapies, asthma therapies, emphysema therapies, respiratory distress syndrome therapies, chronic bronchitis therapies, chronic obstructive pulmonary disease therapies, organ-transplant rejection therapies, therapies for tuberculosis and other infections of the lung, fungal infection therapies, and respiratory illness therapies associated with acquired immune deficiency syndrome, an oncology drug, an anti-emetic, and a cardiovascular agent.

74. (Previously Presented) The aerosol composition of claim 20, wherein the nanoparticulate drug particles have an effective average particle size selected from the group consisting of less than about 400 nm, less than about 300 nm, less than about 250 nm, less than about 100 nm, and less than about 50 nm.

75. (Previously Presented) The aerosol composition of claim 22, wherein the drug is selected from the group consisting of proteins, peptides, elastase inhibitors, analgesics, cystic-fibrosis therapies, asthma therapies, emphysema therapies, respiratory distress syndrome therapies, chronic bronchitis therapies, chronic obstructive pulmonary disease therapies, organ-transplant rejection therapies, therapies for tuberculosis and other infections of the lung, fungal infection therapies, and respiratory illness therapies associated with acquired immune deficiency syndrome, an oncology drug, an anti-emetic, and a cardiovascular agent.

76. (Previously Presented) The aerosol composition of claim 22, wherein the nanoparticulate drug particles have an effective average particle size selected from the group consisting of less than about 400 nm, less than about 300 nm, less than about 250 nm, less than about 100 nm, and less than about 50 nm.

77. (Previously Presented) The aerosol composition of claim 30, wherein the drug is selected from the group consisting of proteins, peptides, elastase inhibitors, analgesics, cystic-fibrosis therapies,

asthma therapies, emphysema therapies, respiratory distress syndrome therapies, chronic bronchitis therapies, chronic obstructive pulmonary disease therapies, organ-transplant rejection therapies, therapies for tuberculosis and other infections of the lung, fungal infection therapies, and respiratory illness therapies associated with acquired immune deficiency syndrome, an oncology drug, an anti-emetic, and a cardiovascular agent.

78. (Previously Presented) The aerosol composition of claim 30, wherein the nanoparticulate drug particles have an effective average particle size selected from the group consisting of less than about 400 nm, less than about 300 nm, less than about 250 nm, less than about 100 nm, and less than about 50 nm.

79. (Previously Presented) The aerosol composition of claim 31, wherein the drug is selected from the group consisting of proteins, peptides, elastase inhibitors, analgesics, cystic-fibrosis therapies, asthma therapies, emphysema therapies, respiratory distress syndrome therapies, chronic bronchitis therapies, chronic obstructive pulmonary disease therapies, organ-transplant rejection therapies, therapies for tuberculosis and other infections of the lung, fungal infection therapies, and respiratory illness therapies associated with acquired immune deficiency syndrome, an oncology drug, an anti-emetic, and a cardiovascular agent.

80. (Previously Presented) The aerosol composition of claim 31, wherein the nanoparticulate drug particles have an effective average particle size selected from the group consisting of less than about 400 nm, less than about 300 nm, less than about 250 nm, less than about 100 nm, and less than about 50 nm.

81. (Previously Presented) The aerosol composition of claim 33, wherein the drug is selected from the group consisting of proteins, peptides, elastase inhibitors, analgesics, cystic-fibrosis therapies, asthma therapies, emphysema therapies, respiratory distress syndrome therapies, chronic bronchitis therapies, chronic obstructive pulmonary disease therapies, organ-transplant rejection therapies, therapies for tuberculosis and other infections of the lung, fungal infection therapies, and respiratory illness therapies associated with acquired immune deficiency syndrome, an oncology drug, an anti-emetic, and a cardiovascular agent.

82. (Previously Presented) The aerosol composition of claim 33, wherein the nanoparticulate drug particles have an effective average particle size selected from the group consisting of less than about

400 nm, less than about 300 nm, less than about 250 nm, less than about 100 nm, and less than about 50 nm.

83. (Previously Presented) The aerosol composition of claim 35, wherein the drug is selected from the group consisting of proteins, peptides, elastase inhibitors, analgesics, cystic-fibrosis therapies, asthma therapies, emphysema therapies, respiratory distress syndrome therapies, chronic bronchitis therapies, chronic obstructive pulmonary disease therapies, organ-transplant rejection therapies, therapies for tuberculosis and other infections of the lung, fungal infection therapies, and respiratory illness therapies associated with acquired immune deficiency syndrome, an oncology drug, an anti-emetic, and a cardiovascular agent.

84. (Previously Presented) The aerosol composition of claim 35, wherein the nanoparticulate drug particles have an effective average particle size selected from the group consisting of less than about 400 nm, less than about 300 nm, less than about 250 nm, less than about 100 nm, and less than about 50 nm.

85. (Previously Presented) The aerosol composition of claim 35, wherein the aggregates of the nanoparticulate drug particles have a mass median aerodynamic diameter of about 2 to about 10 microns.

86. (Previously Presented) The aerosol composition of claim 85, wherein the aggregates of the nanoparticulate drug particles have a mass median aerodynamic diameter of about 2 to about 6 microns.

87. (Previously Presented) The aerosol composition of claim 35, wherein the aggregates of the nanoparticulate drug particles have a mass median aerodynamic diameter of less than about 2 microns.

88. (Previously Presented) The aerosol composition of claim 35, wherein the aggregates of the nanoparticulate drug particles have a mass median aerodynamic diameter of about 5 to about 100 μm.

89. (Previously Presented) The aerosol composition of claim 88, wherein the aggregates of the nanoparticulate drug particles have a mass median aerodynamic diameter of about 30 to about 60 μm.

90. (Previously Presented) The method of claim 40, wherein the drug is selected from the group consisting of proteins, peptides, elastase inhibitors, analgesics, cystic-fibrosis therapies, asthma therapies, emphysema therapies, respiratory distress syndrome therapies, chronic bronchitis therapies,

chronic obstructive pulmonary disease therapies, organ-transplant rejection therapies, therapies for tuberculosis and other infections of the lung, fungal infection therapies, and respiratory illness therapies associated with acquired immune deficiency syndrome, an oncology drug, an anti-emetic, and a cardiovascular agent.

91. (Previously Presented) The method of claim 40, wherein the nanoparticulate drug particles have an effective average particle size selected from the group consisting of less than about 400 nm, less than about 300 nm, less than about 250 nm, less than about 100 nm, and less than about 50 nm.

92. (Previously Presented) The method of claim 40, wherein the aggregates of the nanoparticulate drug particles have a mass median aerodynamic diameter of about 2 to about 10 microns.

93. (Previously Presented) The method of claim 92, wherein the aggregates of the nanoparticulate drug particles have a mass median aerodynamic diameter of about 2 to about 6 microns.

94. (Previously Presented) The method of claim 40, wherein the aggregates of the nanoparticulate drug particles have a mass median aerodynamic diameter of less than about 2 microns.

95. (Previously Presented) The method of claim 40, wherein the aggregates of the nanoparticulate drug particles have a mass median aerodynamic diameter of about 5 to about 100 μm.

96. (Previously Presented) The method of claim 95, wherein the aggregates of the nanoparticulate drug particles have a mass median aerodynamic diameter of about 30 to about 60 μm.

97. (Previously Presented) The method of claim 42, wherein the drug is selected from the group consisting of proteins, peptides, elastase inhibitors, analgesics, cystic-fibrosis therapies, asthma therapies, emphysema therapies, respiratory distress syndrome therapies, chronic bronchitis therapies, chronic obstructive pulmonary disease therapies, organ-transplant rejection therapies, therapies for tuberculosis and other infections of the lung, fungal infection therapies, and respiratory illness therapies associated with acquired immune deficiency syndrome, an oncology drug, an anti-emetic, and a cardiovascular agent.

98. (Previously Presented) The method of claim 42, wherein the nanoparticulate drug particles have an effective average particle size selected from the group consisting of less than about 400 nm, less than about 300 nm, less than about 250 nm, less than about 100 nm, and less than about 50 nm.

99. (Previously Presented) The method of claim 42, wherein the aggregates of the nanoparticulate drug particles have a mass median aerodynamic diameter of about 2 to about 10 microns.

100. (Previously Presented) The method of claim 99, wherein the aggregates of the nanoparticulate drug particles have a mass median aerodynamic diameter of about 2 to about 6 microns.

101. (Previously Presented) The method of claim 42, wherein the aggregates of the nanoparticulate drug particles have a mass median aerodynamic diameter of less than about 2 microns.

102. (Previously Presented) The method of claim 42, wherein the aggregates of the nanoparticulate drug particles have a mass median aerodynamic diameter of about 5 to about 100 μm.

103. (Previously Presented) The method of claim 102, wherein the aggregates of the nanoparticulate drug particles have a mass median aerodynamic diameter of about 30 to about 60 μm.

104. (Previously Presented) The method of claim 43, wherein the drug is selected from the group consisting of proteins, peptides, elastase inhibitors, analgesics, cystic-fibrosis therapies, asthma therapies, emphysema therapies, respiratory distress syndrome therapies, chronic bronchitis therapies, chronic obstructive pulmonary disease therapies, organ-transplant rejection therapies, therapies for tuberculosis and other infections of the lung, fungal infection therapies, and respiratory illness therapies associated with acquired immune deficiency syndrome, an oncology drug, an anti-emetic, and a cardiovascular agent.

105. (Previously Presented) The method of claim 43, wherein the nanoparticulate drug particles have an effective average particle size selected from the group consisting of less than about 400 nm, less than about 300 nm, less than about 250 nm, less than about 100 nm, and less than about 50 nm.

106. (Previously Presented) The method of claim 43, wherein the aggregates of the nanoparticulate drug particles have a mass median aerodynamic diameter of about 2 to about 10 microns.

107. (Previously Presented) The method of claim 106, wherein the aggregates of the nanoparticulate drug particles have a mass median aerodynamic diameter of about 2 to about 6 microns.

108. (Previously Presented) The method of claim 43, wherein the aggregates of the nanoparticulate drug particles have a mass median aerodynamic diameter of less than about 2 microns.

109. (Previously Presented) The method of claim 43, wherein the aggregates of the nanoparticulate drug particles have a mass median aerodynamic diameter of about 5 to about 100 μm.

110. (Previously Presented) The method of claim 109, wherein the aggregates of the nanoparticulate drug particles have a mass median aerodynamic diameter of about 30 to about 60 μm.

111. (Previously Presented) The method of claim 44, wherein the drug is selected from the group consisting of proteins, peptides, elastase inhibitors, analgesics, cystic-fibrosis therapies, asthma therapies, emphysema therapies, respiratory distress syndrome therapies, chronic bronchitis therapies, chronic obstructive pulmonary disease therapies, organ-transplant rejection therapies, therapies for tuberculosis and other infections of the lung, fungal infection therapies, and respiratory illness therapies associated with acquired immune deficiency syndrome, an oncology drug, an anti-emetic, and a cardiovascular agent.

112. (Previously Presented) The method of claim 44, wherein the nanoparticulate drug particles have an effective average particle size selected from the group consisting of less than about 400 nm, less than about 300 nm, less than about 250 nm, less than about 100 nm, and less than about 50 nm.

113. (Previously Presented) The method of claim 44, wherein the aggregates of the nanoparticulate drug particles have a mass median aerodynamic diameter of about 2 to about 10 microns.

114. (Previously Presented) The method of claim 113, wherein the aggregates of the nanoparticulate drug particles have a mass median aerodynamic diameter of about 2 to about 6 microns.

115. (Previously Presented) The method of claim 44, wherein the aggregates of the nanoparticulate drug particles have a mass median aerodynamic diameter of less than about 2 microns.

116. (Previously Presented) The method of claim 44, wherein the aggregates of the nanoparticulate drug particles have a mass median aerodynamic diameter of about 5 to about 100 μm.

117. (Previously Presented) The method of claim 116, wherein the aggregates of the nanoparticulate drug particles have a mass median aerodynamic diameter of about 30 to about 60 μm.

118. (Previously Presented) The aerosol composition of any one of claims 14, 25, 71, 73, 75, 77, 79, 81, or 83 wherein the drug is selected from the group consisting of a bronchodilator, a corticosteroid, and an anti-fungal.

119. (Previously Presented) The method of any one of claims 90, 97, 104, and 111, wherein the drug is selected from the group consisting of a bronchodilator, a corticosteroid, and an anti-fungal.

120. (Previously Presented) The aerosol composition of claim 14, wherein the drug is selected from the group consisting of beclomethasone dipropionate, naproxen, triamcinolone acetonide, budesonide, and an anti-emetic.

121. (Previously Presented) The aerosol composition of claim 25, wherein the drug is selected from the group consisting of beclomethasone dipropionate, naproxen, triamcinolone acetonide, budesonide, and an anti-emetic.